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ORIGINAL ARTICLE

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Association between serum vitamin D levels and skeletal muscle indices in an older Japanese population: The SONIC study

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Aim: Vitamin D (VD) affects skeletal muscles. The high prevalence of VD deficiency in Japan may lead to decreased skeletal muscle mass and strength, increasing the prevalence of sarcopenia. Therefore, we aimed to investigate the association between serum VD levels and skeletal muscle indices in a Japanese community-dwelling older population.

Methods: We extracted data from the Septuagenarians, Octogenarians, Nonagenarians Investigation with Centenarians (SONIC) study. We analyzed the data for participants in the 70s and 90s age groups. Skeletal mass index (SMI) using bioimpedance analysis, grip strength, walking speed, and serum VD levels using 25-hydroxyvitamin D [25(OH)D] were measured.

Results: We analyzed the data of 310 participants in their 70s and 48 in their 90s. Mean serum 25(OH)D levels were 21.6 ± 5.0 ng/mL in the 70s group and 23.4 ± 9.1 ng/mL in the 90s group. In the 70s group, serum 25(OH)D levels correlated with SMI ($r = 0.21$, $P < 0.0001$) and grip strength ($r = 0.30$, $P < 0.0001$). Serum 25(OH)D levels were independently associated with SMI after adjusting for sex, body mass index, and serum albumin levels. In the 90s group, serum 25(OH)D levels were correlated with SMI ($r = 0.29$, $P = 0.049$) and grip strength ($r = 0.34$, $P = 0.018$). However, the multivariate analysis showed no independent association between SMI, grip strength, and serum 25(OH)D levels.

Conclusion: In a cross-sectional analysis of an older population, serum VD levels were associated with SMI and grip strength, and this association was more pronounced in the 70s group than in the 90s group. Our results suggest that serum VD levels maintain skeletal muscle mass and grip strength. **Geriatr Gerontol Int 2024; ••: ••–••.**

Keywords: grip strength, skeletal muscle, SONIC study, vitamin D.

Introduction

Sarcopenia is characterized by reduced muscle strength and skeletal muscle mass.[1] In a Japanese community-dwelling population aged 65 years or older, 11.5% of men and 16.7% of women met the Asian Working Group for Sarcopenia 2019 (AWGS2019) criteria.[2] After 5.8 years of follow-up, the mortality hazard of sarcopenia was 2.0 times higher in men and 2.3 times higher in women among this population.[2] Several factors have been reported to cause sarcopenia, including age-related changes in nutritional status, decreased activity, and endocrine factors; however, many of these remain unknown. Although adequate protein intake and physical training are recommended to manage sarcopenia,[1] evidence supporting the effectiveness of therapeutic agents for sarcopenia is scarce.

Recently, vitamin D (VD) was shown to influence skeletal muscle development and bone metabolism.[3] A review of various studies reported that VD supplementation may improve sarcopenia.[4] Concurrently, a lack of VD may promote sarcopenia. In Japan, the measurement of serum VD levels has been covered by insurance since August 2016, and the Japan Endocrine Society provided the definitions of VD deficiency and insufficiency in 2017.[5] They defined the criteria for VD deficiency and insufficiency as serum 25-hydroxyvitamin D [25(OH)D] <20 ng/mL and 25(OH)D < 30 ng/mL, respectively. Yoshimura *et al.* reported that more than 80% of Japanese patients with osteoarthritis and osteoporosis met the criteria for VD deficiency.[6] Therefore, VD deficiency and insufficiency may contribute to the development of sarcopenia in older Japanese individuals. However, few studies have examined the association between VD and sarcopenia in community-dwelling older adults.

In this study, we investigated the distribution of serum 25(OH)D levels in participants of the Septuagenarians, Octogenarians, Nonagenarians Investigation with Centenarians (SONIC) study, a cohort study of Japanese community-dwelling older adults, and its relationship with the elements of sarcopenia, namely skeletal muscle index (SMI), grip strength, and walking speed. Furthermore, we investigated these relationships in the 70s and 90s age groups to clarify the effects of age.

Methods

Study design and setting

We extracted data from participants of the SONIC study, a long-term longitudinal epidemiological study of community-dwelling older adults. This study was designed to identify factors associated with health and longevity. The participants were residents of four areas of western and eastern Japan: Itami City, Hyogo (western urban), Asago City, Hyogo (western rural), Itabashi ward, Tokyo (eastern urban), and Nishitama County, Tokyo (eastern rural). They lived independently and were randomly selected from the resident registry. Participants were divided into 70s, 80s, 90s, and 100s age groups and followed up every 3 years. We used local survey sites and examined participants who visited the venues. Detailed information regarding the SONIC study has been published elsewhere.[7] In the current study, we analyzed data of participants in their 90s collected in 2015 and in their 70s collected in 2016, who were residents of Itami City or Asago City. Itami City is located at 34.8° north latitude and 135.4° east longitude, while Asago City is located at 35.3° north latitude and 134.8° east longitude. Participants in their 80s in 2014 were also scheduled to be analyzed but were excluded because the survey did not yield a sufficient number and quality of samples. The study was limited to the 90s in 2015 and 70s in 2016 because we found an adequate sample number and quality. The study protocol was approved by the Institutional Review Board of Osaka University Graduate School of Medicine, Dentistry, and Human Sciences (approval numbers 266, H22-9, and 22 018, respectively). All participants provided written consent after obtaining detailed information on the study. The study was conducted in accordance with the Declaration of Helsinki.

Measurements

The study participants were sedentary and fasted for at least 2 h before blood collection. We used serum 25(OH)D concentrations to assess the VD status in the body. Using a frozen stored serum, H.U. Frontier, Inc. (Tokyo, Japan), we measured serum 25(OH)D concentrations using the radioimmunoassay (RIA) method. In this study, we measured serum 25(OH)D concentrations in 2016. Therefore, the results were obtained using RIA, which was the available method of measurement at that time. We defined VD deficiency as a serum 25(OH)D level of <20 ng/mL, according to the criteria of the Japan Endocrine Society.[5] Albumin and creatinine levels were determined by ordinary biochemical examination of blood samples drawn at the investigation sites.

Body composition was measured using two types of monitoring: an InBody 430 (InBody Co. Ltd, Seoul, Korea) for participants in their 90s examined in 2015 and a MC-780A (TANITA Corporation, Tokyo, Japan) for participants in their 70s examined in 2016. The SMI was calculated by summing the bilateral upper and lower limb lean muscle masses measured by the bioimpedance analysis method and dividing by the square of the height in meters.

Grip strength was measured using a Smedley grip-strength meter (YD-100; Yagami Inc., Nagoya, Japan). We measured the maximum grip strength of the dominant arm twice and used the average value as the grip strength. We considered a grip-strength value of 28 kg or less for men and 18 kg or less for women as reduced grip strength, according to the AWGS2019 criteria.[1]

In this study, we used a regular walking speed as the walking speed. We measured 2.44 m on a flat floor and marked the start and finish points using tape. The participants walked at an average speed from the front of the mark at the start point, passed the spot at the finish point, and stopped beyond it. The assessor accompanied the participant and measured the walking time for a 2.44-m distance with a stopwatch to the nearest 0.1 s. The measurements were taken twice, and walking speed was calculated as m/s from the average of the two measurements.

Statistical analysis

Data were presented as means ± standard deviation or *n* (%). We used the Shapiro–Wilk test for each variable to assess normality, and tested after natural logarithmic transformation for variables with non-normal distributions. We used *t*-tests for continuous variables and chi-square tests for categorical variables to compare the clinical parameters between men and women. Pearson's correlation coefficients were calculated to determine the association between the SMIs and serum parameters. Multiple regression analysis was performed using SMI and grip strength as dependent variables. We selected independent variables, including serum 25(OH)D levels, based on the regression coefficient (R-squared) and Akaike's information criterion, considering the results of Pearson's correlation coefficients. We defined two-sided $P < 0.05$

as statistically significant. All statistical analyses were performed using SPSS Statistics version 25 (IBM, Armonk, NY, USA).

Results

Table 1 shows the clinical backgrounds of the study participants. The mean age of the participants in the 70s group was 75.9 ± 0.9 years, and 168 (54.2%) were men. The mean serum 25(OH)D concentrations were 21.6 ± 5.0 ng/mL, and 111 (35.8%) patients had a VD deficiency. In contrast, the mean age of the participants in the 90s group was 92.5 ± 1.6 years, and 18 (37.5%) were men. The mean serum 25(OH)D concentrations were 23.4 ± 9.1 ng/mL, and 21 (43.8%) participants were VD-deficient. SMI and grip strength were significantly higher in men than in women in their 70s and 90s; however, walking speed did not differ between men and women in either age group. Serum 25(OH)D levels were lower in women than in men in the 70s and 90s groups, and the percentage of participants with VD deficiency was higher in women than in men in their 70s; however, no sex difference was observed in the 90s group. We examined the differences in the participants' serum 25(OH)D levels according to the measurement period (summer and winter). The serum 25(OH)D levels were higher during the summer period only in men in their 70s, with mean serum 25(OH)D levels of 23.8 ± 4.8 ng/mL in summer and 21.2 ± 4.1 ng/mL in winter. No seasonal differences were observed in the serum 25(OH)D levels according to age group or sex.

We analyzed the simple regression for SMI, grip strength, and walking speed as elements of sarcopenia. In participants in their 70s, serum 25(OH)D levels were associated with SMI and grip strength but not with walking speed (Table 2). Among the participants in their 90s, a mutually significant positive correlation existed between grip strength, walking speed, and SMI. Serum creatinine levels were positively correlated with SMI and grip strength. Serum 25(OH)D levels were associated with SMI and grip strength in the 90s group, similar to in the 70s group (Table 3).

Next, multivariate analyses were conducted using SMI and grip strength associated with serum 25(OH)D levels in a simple regression as dependent variables. Tables 4 and 5 show the results of the multiple regression analysis with SMI as the dependent variable for participants in their 70s and 90s. As shown in Table 4, in the 70s group, serum 25(OH)D levels were independently associated with SMI after adjusting for sex, body mass index, and serum albumin concentration. However, this association was not observed in the 90s group, as shown in Table 5. In contrast, when we performed multiple regression analysis with grip strength as the dependent variable, no independent association was found between serum 25(OH)D levels and grip strength in the analysis results for the 70s (Table 6) and 90s (Table 7) age groups.

Discussion

We found that serum 25(OH)D levels correlated with SMI and grip strength in participants from the 70s group. In multiple regression analysis with SMI as the dependent variable, serum 25(OH)D level was an independent factor after adjusting for sex, body mass index, and serum albumin level. However, in multivariate analysis with grip strength as the dependent variable, serum 25(OH)D levels did not show an independent association. Among participants from the 90s group, SMI and grip strength were also significantly correlated with serum 25(OH)D levels. Nevertheless, there was no independent association on multivariate analysis between serum 25(OH)D levels and either SMI or grip strength.

Several studies have examined the associations among VD, skeletal muscle mass, and muscle strength. However, the characteristics of the study participants and definitions of VD insufficiency were diverse. In a study of Tokyo residents aged 65 years or older, Suzuki *et al.* reported that serum 25(OH)D levels were associated with grip strength, time to stand on one leg with eyes open, and walking speed. However, they did not examine the association between VD and skeletal muscle mass.[8] In the Cardiovascular Health Study All Stars, VD deficiency was associated with low grip strength and poor physical performance. However, skeletal muscle mass was not examined.[9] In patients with chronic liver disease, VD deficiency was associated with low grip strength and skeletal muscle mass.[10] Loss of muscle mass and muscle weakness did not coincide, and muscle strength declined before decreasing muscle mass.[11] Therefore, in studies examining the relationship between VD and SMI, the results may differ depending on whether the participant is in a stage of muscle weakness or muscle mass loss. The participants in our study were slightly older than

Table 1 Baseline characteristics of the study participants

	Age group of 70s		Age group of 90s	
	Male ($n = 168$)	Female ($n = 142$)	Male ($n = 18$)	Female ($n = 30$)
Age, years	75.9 ± 0.8	75.9 ± 1.0	92.6 ± 1.6	92.5 ± 1.6
Body height, cm	163.1 ± 6.2	150.7 ± 5.8*	160.1 ± 6.0	145.0 ± 6.3*
Body weight, kg	61.4 ± 8.5	51.0 ± 7.9*	56.6 ± 9.0	45.7 ± 7.2*
Body mass index, kg/m^2	23.0 ± 2.6	22.4 ± 3.1	22.0 ± 2.8	21.8 ± 3.2
Skeletal muscle index, kg/m^2	7.7 ± 0.9	6.3 ± 0.7*	6.8 ± 0.9	5.4 ± 0.6*
Grip strength, kg	31.4 ± 6.1	19.7 ± 4.5*	23.3 ± 6.2	13.5 ± 3.7*
Walking speed, m/s	1.0 ± 0.2	1.0 ± 0.2	0.8 ± 0.2	0.7 ± 0.2
Serum albumin, g/dL	4.4 ± 0.3	4.4 ± 0.3	4.1 ± 0.2	4.2 ± 0.3
Serum creatinine, mg/dL	0.9 ± 0.2	0.7 ± 0.1*	1.1 ± 0.4	0.7 ± 0.2*
Serum 25(OH)D, ng/mL	23.1 ± 4.7	19.8 ± 4.7*	28.2 ± 9.2	20.5 ± 7.8*
VD deficiency, *n* (%)	37 (22.0)	74 (52.1) *	5 (27.8)	16 (53.3)

Note: Data are presented as mean ± SD or *n* (%). 25(OH)D, 25-hydroxyvitamin D; VD, vitamin D. The comparison of values was done using the *t*-test.

*$P < 0.05$ vs. Male.

Table 2 Correlation coefficients among muscle indices and clinical characteristics in the 70s group

	SMI	Grip strength	Walking speed	Albumin	Creatinine	25(OH)D
BMI	0.66*	0.17*	−0.03	−0.06	0.10	−0.06
SMI	–	0.57*	−0.02	−0.14*	0.45*	0.21*
Grip strength	–	–	0.13*	0.03	0.46*	0.30*
Walking speed	–	–	–	0.05	0.04	0.06
Albumin	–	–	–	–	−0.07	0.13
Creatinine	–	–	–	–	–	0.23

Note: Data are Pearson's regression coefficients between the two parameters. BMI, body mass index; SMI skeletal muscle index; 25(OH)D, serum 25-hydroxyvitamin D.

*$P < 0.05$.

Table 3 Correlation coefficients among muscle indices and clinical characteristics in the 90s group

	SMI	Grip strength	Walking speed	Albumin	Creatinine	25(OH)D
BMI	0.45*	0.24	0.18	0.41*	0.06	−0.01
SMI	–	0.77*	0.42*	0.06	0.42*	0.29*
Grip strength	–	–	0.60*	0.07	0.48*	0.34*
Walking speed	–	–	–	0.31*	0.27	0.24
Albumin	–	–	–	–	−0.21	−0.00
Creatinine	–	–	–	–	–	0.24

Note: Data are Pearson's regression coefficients between the two parameters. BMI, body mass index; SMI skeletal muscle index; 25(OH)D, serum 25-hydroxyvitamin D.

*$P < 0.05$.

Table 4 Multiple regression analysis for skeletal muscle index in the 70s group

	β	*t*	*P*
Sex	−0.59	−22.4	<0.001
Body mass index	0.58	23.5	<0.001
Albumin	−0.11	−4.26	<0.001
Serum 25(OH)D	0.066	2.50	0.013

Note: $R^2 = 0.82$. Independent variables were selected by the stepwise method based on the regression coefficient and Akaike's information criterion, considering the results of Pearson's correlation coefficients. 25(OH)D, serum 25-hydroxyvitamin D.

Table 5 Multiple regression analysis for skeletal muscle index in the 90s group

	β	*t*	*P*
Sex	−0.65	−6.60	<0.001
Body mass index	0.45	4.60	<0.001
Albumin	−0.082	−0.83	0.41
Serum 25(OH)D	0.022	0.22	0.82

Note: $R^2 = 0.65$. Independent variables were selected by the stepwise method based on the regression coefficient and Akaike's information criterion, considering the results of Pearson's correlation coefficients. 25(OH)D, serum 25-hydroxyvitamin D.

Table 6 Multiple regression analysis for grip strength in the 70s group

	β	*t*	*P*
Sex	−0.71	−17.6	<0.001
Body mass index	0.093	2.46	0.015
Walking speed	0.19	5.12	<0.001
Serum 25(OH)D	0.065	1.63	0.10

Note: $R^2 = 0.57$. Independent variables were selected by the stepwise method based on the regression coefficient and Akaike's information criterion, considering the results of Pearson's correlation coefficients. 25(OH)D, serum 25-hydroxyvitamin D.

Table 7 Multiple regression analysis for grip strength in the 90s group

	β	*t*	*P*
Sex	−0.57	−5.88	<0.001
Body mass index	0.14	1.60	0.12
Walking speed	0.41	4.44	<0.001
Serum 25(OH)D	0.010	0.11	0.92

Note: $R^2 = 0.68$. Independent variables were selected by the stepwise method based on the regression coefficient and Akaike's information criterion, considering the results of Pearson's correlation coefficients. 25(OH)D, serum 25-hydroxyvitamin D.

those reported in other studies and might have reached the stage of SMI decline more often than grip strength decline. Another possible reason for the association between VD and SMI, but not grip strength, could be the strong correlation between SMI and grip strength, which might have affected our multivariate analysis. Various epidemiological studies have shown that serum 25(OH)D levels are associated with SMI.

The mechanisms underlying the association between VD and SMI are as follows. VD binds to and exerts its function through the nuclear receptor, vitamin D receptor (VDR). Endo *et al.* analyzed systemic VDR-knockout mice and reported that VDR plays a physiological role in skeletal muscle development and controls muscle regulatory transcription factors.[3] VDRs are also expressed

in skeletal muscles, and comparisons between systemic VDR-knockout mice and myocyte-specific VDR-null mice showed that VD signaling is essential for maintaining skeletal muscle size and strength.[12] Mizuno *et al*. noted that VDR signaling contributes to muscle strength maintenance via sarcoendoplasmic reticulum Ca^{2+}-ATPase SERCA 1 and SERCA 2a in mice with a mature muscle fiber-specific VDR knockout.[13] Based on these findings, VD is related to SMI, and further studies are required.

We found that serum 25(OH)D levels in patients in their 70s were lower than in those in their 90s. Two reasons can explain this observation. First, participants in their 70s had a lower VD intake than those in their 90s. Second, there might have been a selection bias for those in their 90s with healthier lifestyles owing to the research method used. Therefore, the results of our study differ from those of other studies.

This study has some limitations. First, its cross-sectional design precludes establishing a cause-and-effect relationship. As clinical populations typically include few patients in their 90s, the study findings may primarily apply to those in their 70s. Second, we did not examine the participants' daily activity levels, sun exposure, or energy intake. A study in young women reported that the number of daily steps correlated with serum 25(OH)D levels.[14] Therefore, the amount of outdoor physical activity may be a confounding factor in SONIC study participants, as it may affect SMI and VD levels. Third, participants in the SONIC study were relatively healthy and independent community residents. Consequently, detailed testing or diagnosis was not conducted. The SONIC study only inquired about the participants' medication use and lacks comprehensive information on drugs or supplements. Therefore, the potential effects of these factors could not be fully assessed. Finally, owing to the absence of fortification in Japanese milk and other foods, average serum vitamin D levels tend to be low. Therefore, the results of this study may not be generalizable to populations in other countries.

In conclusion, this cross-sectional analysis of a community-dwelling older population cohort found that serum VD levels were associated with SMI and grip strength but not with walking speed. In independent older people, the association was more pronounced in the 70s than in the 90s group. Maintenance of serum VD levels may contribute to the maintenance of skeletal muscle mass. Further research is warranted to provide insight into better VD supplementation and maintaining SMI in older adults.

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Disclosure statement

The authors have no financial conflicts of interest to disclose concerning the study.

Author contributions

All authors critically revised the manuscript for important intellectual content and gave their final approval for submission. Additionally, the following authors contributed specifically. YO and HA: collected the data, analyzed the data, and drafted the article. KH, KT, ShY, YY, TF, MI, KG, MiK, MaK, KS, YM, KM, SaY, MO, and TN: data collection. YA, TI: research conception. YG, KI, KK, and KY: study design and data interpretation.

Data availability statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

Ethics statement

The study protocol was approved by the Institutional Review Board of Osaka University Graduate School of Medicine, Dentistry, and Human Sciences (approval numbers 266, H22-9, and 22 018, respectively). The study was conducted in accordance with the Declaration of Helsinki and its later amendments.

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Patient consent statement

Written informed consent was obtained from all participants.

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